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| EXAMINER | |
|---|---|
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/597,935 | FAIS ET AL. | |
| | Examiner | Art Unit | |
| | IVAN GREENE | 1619 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *18 October 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *50-76* is/are pending in the application.

4a) Of the above claim(s) *50 and 59-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/17/2010; 05/24/2010; and 10/18/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election with traverse of Group II, claims 51-60 in the reply filed on 10/18/2010 is acknowledged. The traversal is on the ground(s) that the claims of Group III ( claims 61-68 and 71-75) include methods of treating cancerous conditions and that many of the compounds listed in claim 64 are useful as cancer chemotherapeutic agents. This is not found persuasive because the claims of Group II are drawn to methods of treatment and prophylaxis of a cancerous condition, whereas the claims of Group III are generic to any disease condition. Although the examiner recognizes that the genus of while cancerous conditions fall within the broadly claimed genus, independent claim 61 (of Group III) is not limited to treatment of a cancerous condition.

Applicant's attention is directed to the fact that the application is filed under 35 USC 371. The examiner has provided prior art to show a lack of unity of invention between the claims, as filed. In light of the prior art provided of record, the claims lack the same or corresponding special technical feature and thus, lack unity of invention. The different diseases and conditions available in Group III are distinct from those of Group I and encompass numerous diseases and conditions that are not cancer-related. For example, the claims of Group III are drawn to AIDS, RA, UC, CD, or a combination thereof (compare instant claim 69), whereas, the claims of Group II are drawn to cancerous conditions. Groups II and III comprise patentably distinct alternative embodiments, including different alternative embodiments of diseases and conditions and the claims of Group III do not significantly overlap or encompass the same subject matter as the claims of Group II.

Additionally, Applicant is reminded that the initial election of a Group and alternative embodiments is Applicant's exclusive decision and right. Applicant could have easily elected Group III, encompassing the broader genus of "any disease or condition" and then elected an alternative embodiment of a cancerous condition, which may have brought the scope of Groups II and III into

alignment. This alignment may have been persuasive for consideration of rejoinder based on Applicant's election of alternative embodiments. However, because Applicant chose otherwise, the examiner is bound (at least at the outset) by Applicant's own choice.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election of the following species in the response filed 10/18/2010 is acknowledged: (i) a proton pump inhibitor is omeprazole; (ii) an antacid is bicarbonate; (iii) a cancerous condition is adenocarcinoma; and (iv) a further drug is the anticancer drug cisplatin. The claims of elected Group II that read on the elected species are claims 51-58.

Claims 50 and 59-76 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/18/2010.

### *Objection to the Specification*

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The use of the word "novel" in the title is objected to. The determination of novelty is a matter for examination is not appropriate for the title of an application undergoing examination. Moreover, the prior art cited of record and herein clearly shows that the titled use as presently presented is not, in fact, "novel."

The following title is suggested: Method of using proton pump inhibitors in combination with other medicaments.

### *Claim Rejections*

#### *Claim Rejections - 35 U.S.C. 112 - First Paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Claims 51-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "treatment of a cancerous condition", does not reasonably provide enablement for "prophylaxis" (read as prevention) of a cancerous condition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.**

The term "prophylaxis" is defined by Webster's Collegiate Dictionary as follows:

**pro·phy·lac·tic** \ˌprō-fə-ˈlak-tik *also* ˌprä-\ *adj* [Gk *prophylaktikos,* fr. *prophylassein* to be on guard, fr. *pro-* before + *phylassein* to guard, fr. *phylak-, phylax* guard] (1574) **1** : guarding from or preventing the spread or occurrence of disease or infection **2** : tending to prevent or ward off : PREVENTIVE — **pro·phy·lac·ti·cal·ly** \-ti-k(ə-)lē\ *adv*
**prophylactic** *n* (1642) : something prophylactic; *esp* : a device and esp. a condom for preventing venereal infection or conception
**pro·phy·lax·is** \-ˈlak-səs\ *n, pl* **-lax·es** \-ˈlak-ˌsēz\ [NL, fr. Gk *prophylaktikos*] (ca. 1842) : measures designed to preserve health (as of an individual or of society) and prevent the spread of disease

Prophylaxis is a term which clearly encompasses prevention. This definition is in accord with the use of the term in the specification (see, i.e. p. 10, which discusses treatment of hereditary cancer on a prophylactic (i.e. read as preventative) basis).

Applicant claims a composition comprising a proton pump inhibitor and an antacid, and methods for the prophylaxis of a cancerous condition by the oral administration of said composition. Therefore the scope of the instantly rejected claims embraces using a proton pump inhibitor and an antacid for the "prevention of a cancerous condition." A limitation that, in view of the prior art and the disclosed invention, is not reasonably enabled.

The prior art teaches proton pump inhibitors may reduce tumor cell resistance to cytotoxic chemotherapeutic agents (DE MILITO, Expert Opinion on Pharmacotherapy, 6(7), pp. 1049-1054). The

prior art further teaches that mechanism underlying the tumor cell resistance to cytotoxic chemotherapeutic agents includes the overexpression of P-glycoprotein, a cellular plasma membrane efflux transporter, and the alteration of the tumor cell microenvironment via changes is the pH gradient between the extracellular environment and the cell cytoplasm (LUCIANI, Journal of the National Cancer Institute, Vol. 96, No. 22, pp. 1702-1713). The prior art suggests that the second mechanism may be disrupted by the use of proton pump inhibitors. While the prior art does suggest that proton pump inhibitors may be useful for treating tumor cells (cancer), there is no teaching or suggestion that proton pump inhibitors can prevent the occurrence of cancer.

The instant specification discloses the compositions of the instant invention as useful for the prophylaxis of hereditary cancer, or a cancerous condition ([0055] to [0059], as published; and p. 10). The instant specification does not provide any experimental evidenced that the inventive compositions can be useful for the prophylaxis of a cancerous condition. The instant specification suggests that the "prophylaxis of stomach cancer will differ from treatment of an ulcer, in that it must be continued indefinitely," but fails to provide any guidance as to as suitable dose or prophylaxis regime. The instant specification suggests that the dose should be suitable to raise the pH of a microenvironment associated with a cancerous condition, however this would provide no guidance to a person having ordinary skill in the art in developing a dose and regime for the prophylaxis because said microenvironment does not yet exist.

Therefore a person having ordinary skill in the art would not know where to begin to develop a dose or prophylaxis regime for a cancerous condition and the level of experimentation would have been undue experimentation. And the instantly claimed "prophylaxis of a cancerous condition" is not reasonably enabled.

Additionally, the specification does not reasonably provide enablement for prophylaxis (prevention) of cancer in any species by any means. The skilled artisan cannot envision the prevention of

cancer. Prevention involves "attacking" the underlying cause of the cancer; i.e., disrupting the mechanisms which give rise to the cancer. The skilled artisan is aware that the causes of cancer were not completely known at the time of the invention herein. For purposes of enablement, the specification must provide reasonable detail in order for those skilled in the art to carry out the invention. In this case, the specification must disclose a means of preventing cancer regardless of the underlying causes of cancer. The teachings of the specification do not enabled a person of ordinary kill in the art to make and use the claimed method of prophylaxis. Moreover, "[p]atent protection is granted only in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable." *Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d at 1366, 42 USPQ2d at 1005 (Fed. Cir.), cert. denied, 118 S. Ct. 397 (1997), ("Tossing out the mere germ of an idea does not constitute an enabling disclosure").

Reasonable guidance with respect to preventing cancer relies on quantitative analysis from defined populations which have been successfully pre-screened and are predisposed to particular types of cancer. This type of data might be derived from widespread genetic analysis, clusters, or family histories. The essential element towards the validation of a preventive therapeutic is the ability to test the drug on subjects monitored in advance of clinical disease and *link* those results with subsequent histological confirmation of the presence or absence of disease. This irrefutable link between antecedent drug and subsequent knowledge of the prevention of the disease is the essence of a valid preventive agent. However, in the instant case, none of that information is provided by the specification or the prior art, as directed for prevention or prophylaxis.

### ***Claim Rejections - 35 U.S.C. 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**Claims 51-55 are rejected under 35 U.S.C. 102(b) as being anticipated by SARTORI (Journal of Clinical Oncology, Vol. 18, No. 3, pp. 463-467; published February 2000).**

SARTORI discloses a clinical trial in which 300 patients with breast or colon carcinoma[1] (malignant tumor) were randomly assigned pretreatments of 20 mg of omeprazole once a day one week before chemotherapy was started (p. 464, col. 1 § "Study Design"). The chemotherapy consisted of cyclophosphamide, methotrexate, and fluorouracil (CFM) for the breast cancer patients; and fluorouracil alone for the colon cancer patients (i.e. having an adenocarcinoma) (p. 463, col. 2, lines 3-6). The purpose of the clinical trial was to determine if proton pump inhibitors were effective in the prevention of chemotherapy induced damage to the upper gastrointestinal tract (abstract, p. 463, col. 1, lines 1-21). the conclusion of the study was that omeprazole was effective in preventing chemotherapy induced gastroduodenal injury (abstract).

The limitation "for the treatment or prophylaxis of a cancerous condition" has been regarded as an intended use and thus not limiting the invention as currently claimed. The MPEP § 2106 (II) (C.) indicates:

> The subject matter of a properly construed claim is defined by the terms that limit its scope. It is this subject matter that must be examined. As a general matter, the grammar and intended meaning of terms used in a claim will dictate whether the language limits the claim scope. Language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation. The following are examples of language that may raise a question as to the limiting effect of the language in a claim: (A) statements of intended use or field of use…

Also see MPEP § 2111.03 (II) for a discussion of preamble statements reciting intended use.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 56-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over SARTORI as applied to claims 51-55 above, and PHILLIPS (US 20030191159, 9 October 2003, benefit to 19 January 2002; issued as US 6,699,885; 2 March 2004, benefit to 19 January 2002).**

SARTORI disclose a clinical trial in which patients are administered the proton pump inhibitor omeprazole as a pretreatment aimed at preventing gastroduodenal injury due to chemotherapy for the treatment of carcinoma, as discussed above.

SARTORI does not teach the administration of the antacid species calcium carbonate.

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[1] See College of American Pathologist information sheet on "Colon Cancer" which indicates that the most common

PHILLIPS teaches a methods of administering pharmaceutical composition comprising a proton pump inhibitor (omeprazole) and calcium carbonate wherein, upon administration to a patient in need thereof, the calcium carbonate raises the gastric pH and the higher pH environment produced by the calcium carbonate allows for the partial or complete dissolution of the enteric coating by the gastric fluid allowing for the omeprazole to be available for immediate absorption into the bloodstream (12:56-67; 13:1-2).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to pre-administer an antacid drug such as calcium carbonate with an enteric coated omeprazole formulation, as suggested by PHILLIPS, because the calcium carbonate would raise the stomach pH enabling the rapid dissolution of the omeprazole in the lower pH environment of the stomach where it is most effectively absorbed. The motivation to provide a calcium carbonate with or before the enteric coated omeprazole would have been the enhanced absorption of the omeprazole at the lower stomach pH. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention in light of the express teachings of PHILLIPS.

Moreover, commercially available over-the-counter compositions of calcium carbonate (sold and marketed under numerous brand names including TUMS and ROLAIDS) and omeprazole (sold and marketed under numerous brand names including PRILOSEC, LOSEC, MOPRAL, GASTROLOC, ANTRA, ZEGERID, SEGAZOLE, ULCOZOL, and XELOPES, to name a few) are available as over-the-counter medicaments (see especially TUMS, ROLAIDS, and PRILOSEC in the US) and are used for the same purpose (to raise stomach pH). "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been

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type of gastrointestinal cancer is colon adenocarcinoma.

individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) and *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) (mixture of two known herbicides held *prima facie* obvious). Based on the teaching of the prior art and obvious commercially available over-the-counter compositions like TUMS, ROLAIDS, and PRILOSEC (omeprazole), which both functionally act to raise stomach pH, a combination of the two medicaments would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the express teachings of PHILLIPS.

***Conclusion***

Claims 51-58 have been examined on the merits. Claims 51-58 are rejected under 35 U.S.C. 112, first paragraph; claims 51-55 are rejected under 35 U.S.C. 102(b); and claims 56-58 are rejected under 35 U.S.C. 103(a). No claims allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to IVAN GREENE whose telephone number is (571)270-5868. The examiner can normally be reached on Monday through Thursday 7AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bonnie Eyler can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

IVAN GREENE
Examiner, Art Unit 1619

/Cherie M. Woodward/
Primary Examiner, Art Unit 1647